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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/368,989	08/05/1999	FRED J. STEVENS	0003/00332	6185

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EXAMINER	
COOK, LISA V	
ART UNIT	**PAPER NUMBER**
1641	25

DATE MAILED: 05/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No. 09/368,989	Applicant(s) STEVENS ET AL.	
	Examin r Lisa V. Cook	Art Unit 1641	

-- The MAILING DATE of this communication appears n the cover sheet with the corresp ndence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-14 and 21-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-0-14 and 21-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *21 October 2002* is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *21* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I (claims 10-14 and 21-31) in Paper No. 24 filed 2/7/03 is acknowledged.

2. Claims 32-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 24. Currently claims 10-14 and 21-31 are under consideration.

OBJECTIONS WITHDRAWN

Drawings

3. The drawings in this application are objected to by the Draftsperson under 37 CFR 1.84 or 1.152 (see PTO-948). Applicant is required to submit a proposed drawing correction in reply to this Office action. However, formal correction of the noted defect can be deferred until the application is allowed.

Applicant's formal drawings filed 10/21/02 in paper #22 to correct the deficiency have obviated the objection. The objection is withdrawn.

OBJECTIONS MAINTAINED

Information Disclosure Statement

4. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

Therefore, unless the examiner on form PTO-892 or applicant on form PTO-1449 lists the references, they have not been considered. Applicant has not addressed the objection, it is maintained.

5. The information disclosure statement filed 21 October 2002 has been considered as to the merits prior to Final Action.

REJECTIONS WITHDRAWN

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

6. Applicants have obviated the rejection of claims 10-14 and 21 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention via amendment or subsequent explanation. The rejections of record in paper# 18 are withdrawn.

Claim Rejections *– 35 USC § 102 and 35 USC § 103*

7. With respect to the claim rejections under 35 U.S.C. 102 and 35 U.S.C. 103, Applicant contends that the reference of Darnell et al. (Molecular Cell Biology, Scientific American Books, copyright 1986, pages 1095-1101) does not teach the instant invention because it contains heavy chains and light chains. This argument was carefully considered and found persuasive.

8. With respect to the reference of Pokkuluri et al. (Structure, 15 August 1998, pp1067-1073), Applicant has submitted Affidavits of Marianne Schiffer and Fred J. Stevens dating the Janusbody constructs reduction to practice as early as March 10, 1998. This argument was carefully considered and found persuasive.

Applicant's arguments have been fully considered and found persuasive.

9. The following rejections are withdrawn:

I. Claims 10–13 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Darnell et al. (Molecular Cell Biology, Scientific American Books, copyright 1986, pages 1095-1101).

II. Claims 10–13 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Pokkuluri et al. (Structure, 15 August 1998, 6, pp1067-1073).

III. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pokkuluri et al. (Structure, 15 August 1998, 6, pp1067-1073) or Darnell et al. (Molecular Cell Biology, Scientific American Books, copyright 1986, pages 1095-1101) in view of in view of Goling (Journal of Immunology, 1980, 124(5), pages 2082-2088)-Abstract Only and Skoog et al. (Scand. J. Immunolgy, 1980, 11(4), pages 369-376)-Abstract Only.

OBJECTION MAINTAINED

Sequence Non-Compliance

10. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

Applicant is given ONE MONTH from the mailing date of this communication within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

Response to Argument

11. Applicant contends that no requirement exists to submit sequence data because the variable light chains, which are modified in the instant invention are well known and available through several public access sites listed in the specification on page 10 lines 9-29 and page 11 lines 1-2. This argument was carefully considered but not found persuasive because although the initial constructs (Len, Rec, Jto, Wil, etc) are well known and identified in the prior art, the inventive modification are not.

Therefore the actual sequence data for the isolated molecule containing two binding site, complementary determining segments, and a linker is required. The rejection is maintained.

NEW GROUNDS OF REJECTION

Claim Objections

12. Claim 11 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 11 requires the first moiety and the second moiety to be light chain variable domains, however this limitation is presently apart of claim 10 as amended. Claim 11 should be canceled.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 10-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 10 is vague and indefinite because it is not clear what applicant means in reciting "at opposite ends of the molecule". Is it Applicants intent to claim the "flip" technique found in the disclosure page 6, lines 1-3 or the β-sheet configuration found in dimer formation. In order to obviate this rejection the β-sheet configuration found in dimer formation should be added to the claims.

B. Claim 23 is vague and indefinite in utilizing the term "Janusbody construct". The term "Janusbody construct" in claim 23 is used by the claim to mean "the binding portions of the construct, or the variable regions of each of the light chain variable regions, counterpoised or otherwise situated at opposite ends of the construct. " As defined on page 5 lines 6-8 of the disclosure. However the term has been created by applicant and as such is not clear to one skilled in the art. As recited the meets and bounds of the claim cannot be meet. It is suggested that the claim include applicant intended meaning of "Janusbody construct".

C. In claims 26-29 are vague and indefinite because it is not known how the recite amino acid substitutions to the molecules listed in claim 24 (Len, Rec, Jto, Wil, Loc, Wat, Cle, Rhe, and combinations thereof) will simultaneously encompass all of the listed molecules. It is not clear how all of the recited molecules will share the same amino acid substitution therein meeting the limitation of the dependent claims 26-29. In other words do all the molecules contain glutamine 38 therein allowing for its substitution to glutamic acid as require by claim 27. Please explain appropriately.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 10-14 and 21-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In particular, claim 10 is drawn to an isolated molecule containing two antigen binding sites and complementary determining segments positioned at opposite ends of the molecule wherein the antigen binding regions are linked to non-binding regions via a peptide linker whereby the moieties are light chain variable domains.

However the mere description of such compositions without the structures (via SEQ ID NO) does not provide possession of the claimed invention. The claims and specification fail to provide the identity or structure of this isolated molecule. The specification does not provide evidence of a sequence identification number meeting/having the descriptive identification. The specification at page 10 lines 9-29 discloses that the structure initially start with known constructs identified in the prior art but were modified to form applicants "Janusbodies". Although the starting materials are found in the prior art, this does not provide adequate description of the final modified constructs. The specification does not state the identity by sequence or any structural characteristics of any other sequence that has the claimed "Janusbodies" characteristics. Moreover, there is evidence that other sequences have not yet been identified (see specification page 5 lines 6-8) therefore; applicants' vague description of an isolated molecule has not been adequately described.

In view of the lack of evidence, it is apparent that Applicants were not in possession of sequences having the described isolated molecule compositions of claim 10, at the time of filing the instant application. The skilled artisan cannot envision the detailed structure of the isolated molecular sequence, thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation.

An adequate description requires more than a mere statement that it is part of the invention. The structure is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. The protein activity characteristics and domain requirements distinguish the protein only by what it does, i.e., protein activity, which are purely functional distinctions. Even where there is an actual reduction to practice, which may demonstrate possession of an embodiment of an invention, it does not necessarily describe what the claimed invention is. The instant specification and claims describe an isolated molecule by its protein function (light variable binding domains), however this description does not describe the claimed isolated molecule itself.

See also, *In The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), where the court held that a generic statement that defines a genus of amino acids/nucleic acids by only their functional activity does not provide an adequate description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of protein/DNA molecules, usually defined by an amino acid sequence or a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". Thus a skilled artisan cannot envision all the contemplated protein/nucleotide sequences by the detailed chemical structure of the claimed polynucleotides and therefore conception cannot be achieved until reduction to practice has occurred.

Thus, in the absence of sequence information of the amino acid, an isolated molecule described only by its protein activity fails to meet the written description requirements. Therefore the full breadth of the claims, have not meet the required written description provision of 35 USC 112, first paragraph.

15. Claims 25-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth a general construct of dimmer light chain variables, however no sequence reciting the specific point mutations are identified. Therefore the written description is not commensurate in scope with the claims drawn to such amino acid substitutions.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117).

The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

The skilled artisan cannot envision the detailed structure of the possible encompassed light chain variable constructs and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The dimer itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of a compound/seq.id/etc. by only their functional activity does not provide an adequate written description of the genus.

The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of molecules, usually defined by a sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description ...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

However, no disclosure, beyond the general dimer compounds is made in the specification. No specific sequence reflecting the particular modifications required in claims 25-31 is disclosed. This is insufficient to support the generic claims as provided by the Interim Written Description Guildlines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore the specific amino acid substitutions claimed would meet the full breadth of the claims as required by the written description provision of 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

16. Claims 10-14 and 21-31 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial, credible or asserted utility or a well-established utility.

Claims 10-14 and 21-31 are broadly drawn to molecules consisting of dual light chain variable domains. The disclosure teaches that the constructs could possibly be utilized as antibodies. However noting that the smallest known functional antibody fragment to date is the variable fragment Fv, which consists of V_H (variable heavy domains) and V_L (variable light domains). See specification page 2 lines 12-19. 14. The specification does not teach a credible utility of the inventive constructs by way of example. The utility of the claimed molecules cannot be linked to the parent antibody without investigative analysis proving such an assertion. Applicant provides guidance for the above noted light variable molecules and provides no guidance as to what modifications or structure are important for the predictable function of any other antibody. Very different structures may be found on antibodies with the same specificity. For example, very different V_H chains can combine with the same V_L chain to produce antibody binding sites with nearly the same size, shape, antigen specificity, and affinity.

A similar phenomenon can also occur when different V_H sequences combine with different V_L sequences to produce antibodies with very similar properties. These observations indicate that divergent variable region sequences, both in and out of complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. Conversely, similar structure may be found on antibodies having different specificities. This is supported by Kabat et al."The role of individual amino acids at various positions is greatly affected by insertions or deletions in the complementarity determining segments". See Journal of Biological chemistry, 1977, 252(19), 6609-6616 – Abstract.

And while the evidence presented in the specification does point to the high probability hat the molecules will function according to their parent antibody structures, this is not sufficient in implementing the same molecules will most certainly share the same function. Protein engineering may result in various forms that may or may not function like the starting molecule. Based on the analysis set forth above the specification does not exemplify sufficient findings that constitute a specific, substantial or credible utility.

Claims 10-14 and 21-31 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by a specific, substantial or credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102((e), f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 10–13, 21, and 22-24 are rejected under 35 U.S.C. 103(b) as being unpatentable over Stevens et al. (Protein Science, 1995, 4:421-432) in view of Berry et al.(WO 96/27612).

Stevens et al. teach variable light chain structure. Sequences of synthetic genes coding for amyloidgenic proteins REC, SMA, and Len were constructed. The variable domains were expressed in *E. Coli* and further provided a system for biophysical and structural comparison of these light-chain proteins. See abstract.

In one embodiment a clone containing the human germline kIV V-segment exon and expression vector pASK40 (two antigen binding sites) were used to construct a plasmid that encoded a germline-type VkIV domain (complementary determining segments). From this template plasmids encoding LEN Vl, SMAVL, and REC were generated. Page 424 1st column. The constructs met the limitations of the instantly claimed invention, see figure 3. Although the reference does not specifically recite that the constructs are Janusbody, the compounds inherently teach these compositions as defined in the specification on page 5 lines 6-9 / "dimeric assembly of two single light chain variable". Stevens et al. teach light chain dimmer formation on page 427 2nd column.

Stevens et al. differ from the instant invention in not specifically teaching the utility of peptide linkers to join antigen binding regions and non-binding regions.

Berry et al. (WO 96/27612) disclose antibody fragments connected by a linking peptide. Portions of antibody light and heavy chains, especially Fv fragments are expressed as a single peptide chain connected by a linking peptide. The peptides linker can be cleaved. In this way both chains are produced in equal amounts but as separate entities. See abstract. In figure 13 and 14 variable light chain regions are bound via peptide linkers (Link1/1st non binding region, Link2/2nd non-binding region, Link3/petide linker). The peptide link (central LINKER 3) is taught to extend from the N-terminal of V_{L1} and the C-terminal of V_{L2} in figure 15. See page 25 lines 15-17. Therein meeting the limitations of claim 22.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the peptide linker as taught by Berry et al. (WO 96/27612) in the isolated variable chain constructs of Stevens et al. because Berry et al. (WO 96/27612) taught that the linkers make the two-chain constructs more stable (page 5 lines 9-14), are more specific (page 6 lines 1-2), and maintains variable domain properties while improving binding properties (page 4 lines 18-20).

One of ordinary skill would have been motivated to incorporate the peptide linkers of Berry et al. (WO 96/27612) to take advantage of the antibody stability/resistant and dual peptide activity/specificity/characteristics. Page 4 lines 7 through page 6 line 16.

II. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stevens et al. (Protein Science, 1995, 4:421-432) in view of Berry et al.(WO 96/27612) as applied to claims 10–13, 21, and 22-24 above, and further in view of Goling (Journal of Immunology, 1980, 124(5), pages 2082-2088)-Abstract Only and Skoog et al. (Scand. J. Immunolgy, 1980, 11(4), pages 369-376)-Abstract Only.

Please see Stevens et al. (Protein Science, 1995, 4:421-432) in view of Berry et al.(WO 96/27612) as set forth above.

Stevens et al. in view of Berry et al. differ from the instant invention in not specifically reciting the weight requirements of claim 14. (between 20,000 and 30,000 daltons).

However, both references of Goling and Skoog et al. teach that the protein structure in the range of 20,000 to 30,000 daltons is important in surface receptor, immunogobulin activity.

Stevens et al., Berry et al., Goling, and Skoog et al. are analogous art, because all four references teach methods concerning protein structures.

Therefore, it would have been obvious at the time the invention was made to a person having ordinary skill in the art to utilize a molecule weighing between 20,000 and 30,000 daltons as taught by Goling and Skoog et al. in the method/product of Stevens et al. in view of Berry et al. to produce a dimeric antigen binding molecule.

A person of ordinary skill in the art would have had a reasonable expectation of success utilizing such compounds, because such weight ranges were previous demonstrated. One of ordinary skill in the art would have been motivated to do this because Goding taught that protease cleavage of the lymphocyte surface IgG typically resulted in one light chain disulfide bond fragment weighting 30,000 daltons. Skooog et al. further taught that SDS polyacrylamide gel electrophoresis exhibited a broad peak at the molecular weight range of 20,000-35,000 daltons for surface receptors.

Response to Arguments

18. The affidavit filed on 21 October 2002 under 37 CFR 1.131of Marianne Schiffer is sufficient to overcome the Pokkuluri et al. reference.

19. The affidavit filed on 21 October 2002 under 37 CFR 1.131of Fred J. Stevens is sufficient to overcome the Pokkuluri et al. reference.

20. For reasons aforementioned and already of record, no claims are allowed.

Remarks

21. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure: Both references disclose general procedures relative to multivalent molecule production in order to increase stability and specificity.

A. Pluckthun et al (Immunotechnology 3, 1997, 83-105)

B. Raag et al. (FASEB, J, 9, 1/1995, pages 73-80)

22. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Lisa V. Cook
Patent Examiner
Art Unit: 1641
CM1 7B17
703-305-0808
4/16/03

LONG V. LE
SUPERVISORY PATENT EXAMINER
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05/04/03